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Quantifying Tissue Heterogeneity using Quadtree Decomposition

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***Abstract*— Volumetric computed tomography (CT) imaging provides a three-dimensional map of image intensities from which lung soft tissue density distribution can be estimated. The information gained from analyzing these images can prove valuable in diagnosis of conditions where lung tissue is damaged or has degenerated, and it is also necessary for modeling lung tissue mechanics. This paper presents a new technique for quantifying heterogeneity based on individual CT images, and investigates the heterogeneity of lung tissue in a group of healthy young subjects. It is intended that development of this technique leads to a standard model of classifying heterogeneity in lung tissue, while taking into account variables such as different imaging platforms and resolutions, and the position of the patient during imaging.**

I. Introduction

Heterogeneity in lung tissue density and vascular perfusion have been suggested as early markers of lung disease [1]. However, the normal lung also exhibits significant heterogeneity hence separating physiology from pathophysiology is difficult. Several methods exist for quantifying pulmonary heterogeneity, however the values reported are dependent on image resolution, and they do not take into account the spatial distribution of heterogeneity [2, 3]. Here we consider an alternative method for quantifying heterogeneity that has the potential to resolve these issues. The method has not previously been applied to lungs.

The quadtree decomposition is a commonly used algorithm in computer science and image processing, for applications such as data partitioning and texture analysis [4]. The technique works in a 2-dimensional image-space by recursively partitioning an image into boxes until all the pixels in each box are considered similar, based on some comparison. The form of comparison used is often a test of homogeneity, such as testing whether all the pixels in a box fall into a given intensity range. If this condition is satisfied, the box is not decomposed any further. Fig. 1 illustrates a quadtree decomposition on a simple shape. We present a method for determining tissue heterogeneity in lung images using the quadtree decomposition algorithm (QTD), and discuss the challenges in developing a general model that can be used for characterizing heterogeneity.

II. Methods

Volumetric multi-detector row computed tomography (MDCT) imaging of the lung was acquired from the University of Iowa Comprehensive Lung Imaging Centre (I-Clic), as part of the Human Lung Atlas initiative [5, 6].

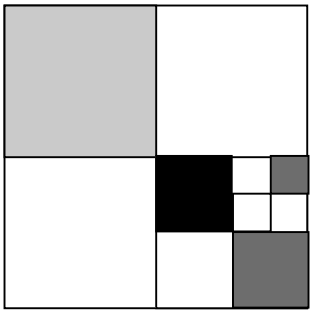

Fig. 1: A quadtree decomposition of a simple heterogeneous shape. 10 distinct boxes are formed.

Imaging of subjects for this study has been approved by the University of Iowa Institutional Review Board and Radiation Safety Committees. Imaging was acquired supine, from 8 healthy 'normal' subjects (4 male and 4 female), all under the age of 40. Imaging was acquired at end expiration (volume-controlled at 55 % vital capacity) and end inspiration (80 % vital capacity).

A. Lung Segmentation

For each subject, the lungs, major airways, and vessels were automatically segmented (Fig. 2b) using the custom-built software package PASS (Pulmonary Analysis Software Suite, University of Iowa) [6, 7].

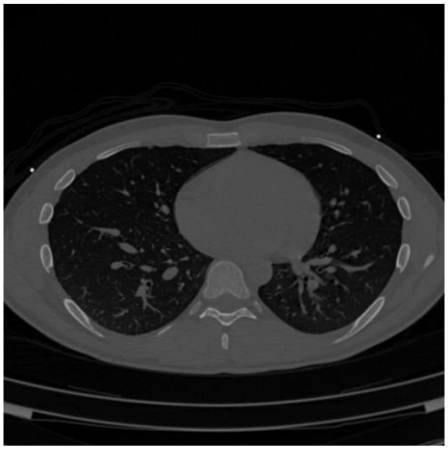

Fig. 2a: An original lung MDCT image

Fig. 2b: The segmented lung image's mask

The original DICOM images and resultant masks from segmentation were then loaded into MATLAB (version 2010a, The MathWorks Inc.). The masks were applied to the raw images and all non-lung data in the images was subtracted. An erosion filter was used to remove noise from the edges of the resultant lung tissue images. These images were then used as the basis for further analysis.

B. Heterogeneity Analysis

A new metric for lung tissue heterogeneity was calculated by selecting individual MDCT images and processing them with the QTD using MATLAB. Images were selected at locations along the cranial-caudal axis at positions of 25%, 50%, and 75% of the height of the lung (incrementing from cranial to caudal) (Fig. 3).

The pixel intensity values in a typical lung image correspond to density in Hounsfield units (HU), with values of approximately -1000 (for air density) and zero (for water density) [7]. Blood, bone, and other tissue are calibrated to have intensities of 40 and above. The QTD was programmed to exclude regions of high pixel values corresponding to blood and tissue, so as to avoid boxes being created due to edge effects between vessels and lung tissue. Box decomposition was performed based on the range of pixel intensities within a box, so that boxes were decomposed if the intensity range of a given box exceeded 100 (corresponding to approximately 10 % of the useful range of HU values present in an MDCT image). Fig. 4a shows a standard segmented lung image, and Fig. 4b illustrates its QTD result.

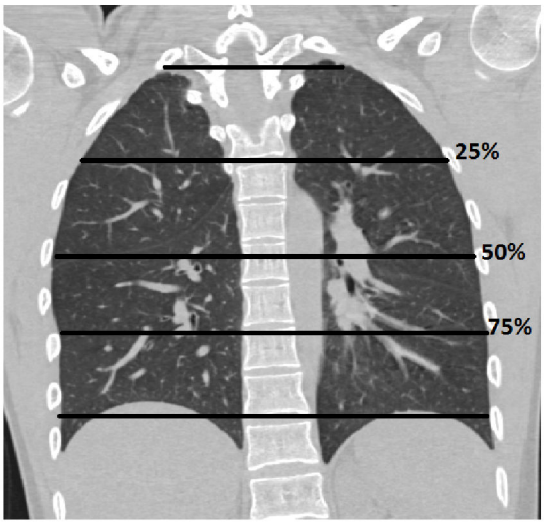

Fig. 3: Slices taken in the cranial-caudal axis for heterogeneity measurements

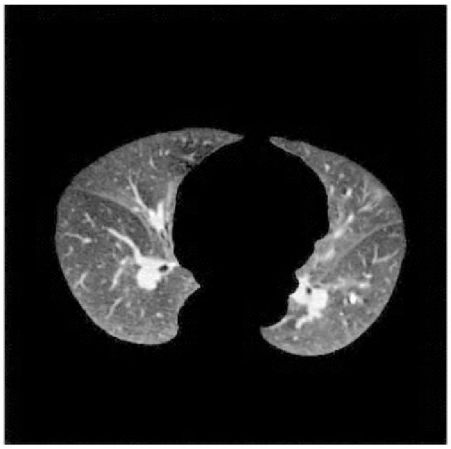

Fig. 4a: A masked lung MDCT image

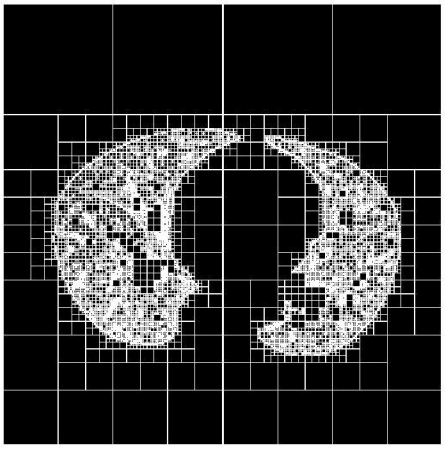

Fig. 4b: The lung image's Quadtree Decomposition

The number of boxes (N) created in this manner ranges from 10,000 to 20,000, so the boxes outside the lung tissue area need not be removed as the quantity is negligible. The total number of boxes was calculated from the QTD's resultant matrix, and this value was normalized by the lung's area. Area was calculated by summing the number of pixels in the lung image's footprint. The time taken for a single image to be processed by the QTD is 1 to 2 seconds. The initial heterogeneity metric is therefore h_{QTD} = N/Area.

We hypothesized that h_{QTD} would decrease with lung inflation. To test this hypothesis, heterogeneity was calculated using the QTDs for the three equally spaced images at end inspiration and end expiration. h_{QTD} values are plotted in Fig. 5, illustrating a reduction in heterogeneity from end expiration to end inspiration. A paired student's t-test performed for each subject on the mean values for the two volumes yields a p-value of 0.0001, indicating that h_{QTD} is statistically different for the two volumes, for each individual. An unpaired test between the groups yields a p-value of 0.0018, indicating that the means of the two groups are also statistically different, and the groups are distinct.

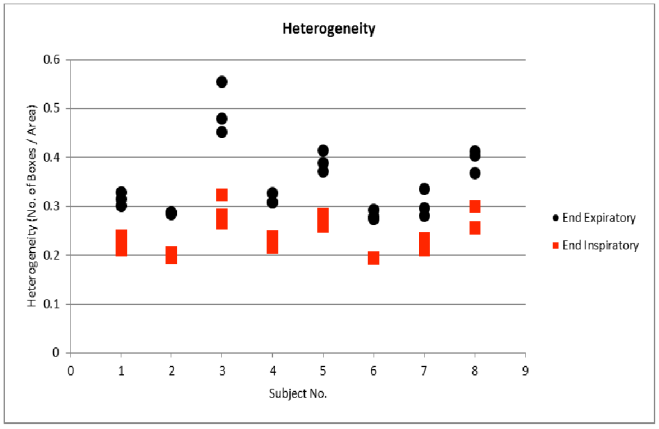

Fig. 5: Subject heterogeneities at end expiration and end inspiration.

C. Image Resolution Analysis

The heterogeneity values reported in Fig. 5 were calculated when the technique was performed on MDCT images of size 512x512, however different imaging modalities have different typical resolutions. For this algorithm to be used with other imaging methods, we therefore need to understand how resolution affects the calculated h_{QTD}. To simulate the effect of scaling an image to a different resolution, the 512x512 images were reduced to 256x256, 128x128, and 64x64 pixels, after which they were scaled up to 512x512 again, in order to produce a blurred image (presumably with lower heterogeneity). The resultant values for h_{QTD} are plotted against the sizes to which the 512x512 image was reduced in Fig. 6.

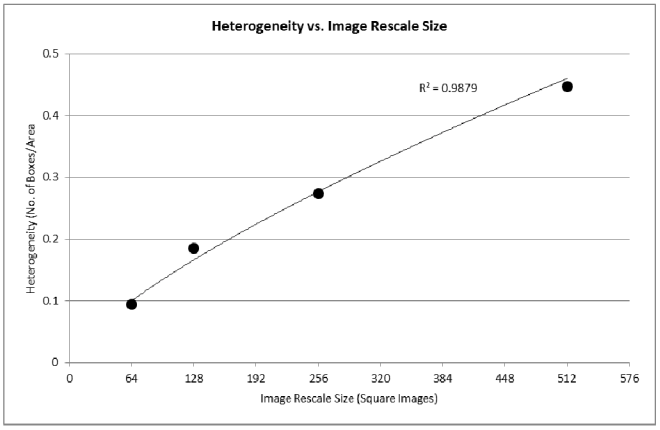

Fig. 6: Resultant heterogeneity of blurred images

C. Box Decomposition Parameters

The Quadtree technique was used with the condition that boxes were divided if the pixel intensity range was greater than 10% of the full intensity range of the image. Boxes were excluded from decomposition if the pixel intensity range within a box was less than 10% of the full intensity range, or the pixels had the high intensity values associated with blood/tissue only. To determine how the threshold influences the calculation of heterogeneity, the threshold was increased as a proportion of the full intensity range of the image, and plotted against the resultant h_{QTD} values. The characteristic curve of the results is shown in Fig. 7, illustrating the non-linear relationship between threshold parameters and heterogeneity.

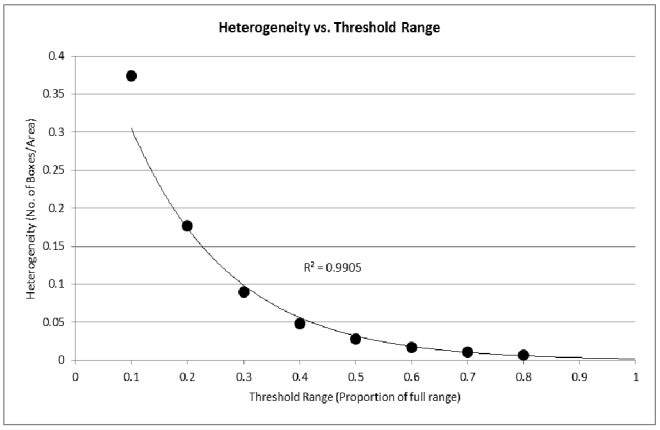

Fig. 7: Resultant heterogeneity values with different threshold bracket sizes

III. Discussion

Quadtree decomposition appears to be a useful method for quantifying lung tissue density heterogeneity. This type of analysis has benefit over existing coefficient of variation or fractal-based methods because it explicitly accounts for the size of regions through which the tissue has similar density. This initial study has shown that end-inspiratory and end-expiratory heterogeneities can be distinguished from each other, across 8 subjects.

In order to make the current methodology more robust in its application across different imaging techniques, it would

be ideal to incorporate the effects of the threshold proportion and imaging resolution into the calculation of heterogeneity. Exactly how this should be done remains to be determined, however the approximately linear relationship between image resolution and heterogeneity (Fig. 6) provides reassurance that heterogeneity scales with image resolution in a reasonable and predictable manner. Furthermore, the relationship between heterogeneity and threshold follows a nonlinear relationship that could potentially be used to relate analyses of subjects that are performed using different threshold criteria.

We have not yet systematically addressed the manner in which heterogeneity changes throughout the lung volume. Although heterogeneity does vary within a lung slice, it has not yet been investigated whether there is a pattern of variation along any of the axes through the lung. The QTD is most likely to reveal differences in heterogeneity in the gravity-dependent axis, because of differences in the extent of tissue expansion due to gravitational deformation of the tissue.

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